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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/866,034	05/25/2001	David Botstein	P2930R1C1	4767

9157 7590 03/20/2003

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EXAMINER
SPECTOR, LORRAINE

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 03/20/2003

13

Please find below and/or attached an Office communication concerning this application or proceeding.

[redacted]

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This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 12/17/02

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 27, 28, 32-35 is/are pending in the application.
Of the above, claim(s) _____ is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☒ Claim(s) 27, 28, 32-35 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of Reference Cited, PTO-892
☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 9
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

Part III: Detailed Office Action

Claims 27-28 and 32-35 are pending and under consideration.

Formal Matters:

The disclosure is objected to because of the following informalities: There are two tables designated "Table 6", the first at page 73, the second at page 114 of the specification. Tables must be numbered consecutively. Applicants are required to correct the numbering of the table at page 114, as well as all subsequent tables, including amending all references in the specification to such tables accordingly.

Appropriate correction is required.

Objections and Rejections under 35 U.S.C. §112:

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 27-28 and 32-35 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well established utility for reasons cited in the previous Office Action, mailed 6/14/02, at page(s) 2-4.

Applicants arguments in paper number 12, filed 12/20/02, have been fully considered but are not deemed persuasive.

With regard to significance of ΔCt values, Applicants argue that it is well known how to calculate ΔCt values, and that the specification teaches that the "diluted samples were used provided that the Ct value of the normal human DNA subtracted from test DNA was +/- 1 Ct." This argument has been fully considered but is not deemed persuasive because, following applicants arguments, a ΔCt value of 1 indicates that the sample had a two-fold amplification of the test sequence as

compared to the control. However, as stated in applicants arguments, the samples were considered to be "comparable" if the normal and test DNA had Ct values of ±1, i.e. a ΔCt value of 1. Accordingly, a ΔCt value of 1 cannot be considered to be a significant difference. As stated in the previous Office Action, it is further noted that the ΔCt values at page 117 are expressed (a) with values to one one-hundredth of a unit (e.g. 2.58), and (b) that only one sample, "LT19", gave values that were consistently (at least on a sample size of 2) at least 2. The Examiner reiterates that it is not clear how measurements of hundredths of a PCR cycle can be made, nor what the significance of a difference of 1 or 2 PCR cycles would be. In this case, as the samples may have an experimental error ΔCt value of ±1 based upon the disclosure that the "diluted samples were used provided that the Ct value of the normal human DNA subtracted from test DNA was +/- 1 Ct," hence the significance of the ΔCt values of approximately 1 are of questionable significance, and it is not clear what the experimental error is (again, what is the significance of a ΔCt value expressed to hundredths of a PCR cycle?). Accordingly, the Examiner cannot determine whether a ΔCt value of 1 is actually within experimental error of being identical, or actually represents a two-fold amplification, or whether a ΔCt value of 2 indicates a 2- or a 4- fold amplification. Given the paucity of information, the Examiner maintains that the data do not support the implicit conclusion of the specification that PRO1800 shows a positive correlation with lung and colon cancer, much less that the levels of PRO1800 would be diagnostic of such. Further, applicants arguments have failed to address the issue of aneuploidy of the test samples as raised in the previous Office Action: As stated in the previous Office Action,

> Even *if* the data demonstrated a slight increase in copy number of PRO1800 nucleic acids in primary tumors, such would not be indicative of a use of the encoded polypeptide as a diagnostic agent. Cancerous tissue is known to be aneuploid, that is, having an abnormal number of chromosomes (see Sen, 2000, Curr. Opin. Oncol. 12:82-88). The data presented in the specification were not corrected for aneuploidy. A slight amplification of a gene does not necessarily mean overexpression in a cancer tissue, but can merely be an indication that the cancer tissue is aneuploid. The preliminary data were not supported by analysis of mRNA or protein expression, for example. Thus, the data do not support the implicit assertion that PRO1800 can be used as a cancer diagnostic. Significant further research would have been required of the skilled artisan to determine whether PRO1800 is overexpressed in any cancer

to the extent that it could be used as a cancer diagnostic, and thus the implicitly asserted utility is not substantial.

Applicants arguments fail to address these points.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 27-28 and 32-35 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 33-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 33-34 depend from canceled claim 22.

Rejections over Prior Art:

A search of the protein sequence databases revealed the following prior art:

[redacted]

Locus	Date	Author	Identity to SEQ ID NO:2
Q9BTZ2	2/01	Strausberg	100%
Q9H3N5	6/00	Furukawa	100%, residues 19-278
O95162	5/1/99	Fransen	99.2%, residues 19-278
AF044127	5/27/99	Fransen	99.3% (1 conservative sub.)

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 27-28, 32 and 35 are rejected under 35 U.S.C. 102(a) as being anticipated by Strausberg, locus Z9BTZ2. As summarized above, the protein of Strausberg is 100% identical to the entirety of SEQ ID NO:2.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 27-28, 32 and 35 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Fransen et al. locus AF044127 for reasons of record.

Applicants sole argument pertaining to the art rejections is that the invention has utility and is therefore entitled to the priority date of 2/11/00. This argument has been fully considered but is not deemed persuasive because the Examiner has maintained a lack of utility in the rejections above.

As the claimed subject matter is found to lack utility and enablement under 35 U.S.C. § §101 and 112, first paragraph, respectively, the effective priority date for this application remains the instant filing date, 5/25/01.

The art made of record and not relied upon is considered pertinent to applicant's disclosure. The National Cancer Institute publishes guidelines for development of cancer markers, at http://www.cancerdiagnosis.nci.nih.gov/assessment/progress/markerdev.html.

Advisory Information:

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory

period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Lorraine M. Spector, whose telephone number is (703) 308-1793. Dr. Spector can normally be reached Monday through Friday, 9:00 A.M. to 5:30 P.M.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Gary L. Kunz, at (703)308-4623.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist at telephone number (703) 308-0196.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Official papers filed by fax should be directed to (703) 872-9306 (before final rejection) or (703)872-9307 (after final). Faxed draft or informal communications with the examiner should be directed to (703) 746-5228.

Lorraine Spector

Lorraine Spector, Ph.D.
Primary Examiner

LMS
09/866034.2
3/18/03

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